

SCIENTIFIC RATIONALE FOR THE POTENTIAL EFFICACY OF HBO2 IN SEVERE TBI

- For nearly three decades and despite multiple randomized trials, there remains no specific treatment for severe TBI victims, unlike conditions stroke and heart attack for which there are specific treatments (thrombolytics and angioplasty).
- Although the brain is only 2% of the total body weight, its extremely high metabolic activity consumes 20% of the oxygen and 25% of the glucose provided by blood flow to the body.
- Following a severe traumatic brain injury, the brain swells which causes a reduction in normal blood flow and oxygen to the injured areas of the brain. Without this proper blood flow and oxygen supply, the injured areas of the brain begin to experience additional brain cell death. The first five days after the initial injury are the most critical to maintain proper blood flow and oxygen supply that will help minimize this cascade of additional brain cell death.
- Hyperbaric oxygen provides oxygen under pressure, allowing the delivery of a very high level of oxygen that is far beyond the normal 100% oxygen delivered, for example, in the ER or ICU on a ventilator.
- This extra high level of oxygen delivered by a hyperbaric oxygen treatment delivers high concentrations of oxygen to the injured areas of the brain, improving brain metabolism and preventing further brain cell death.
- Several animal model studies and human clinical trials of hyperbaric oxygen in severe TBI, performed by a number of different investigators have found this treatment to be efficacious in preventing death and improving neurologic function (see below for additional details and citations).
- This trial and the use of hyperbaric oxygen are both carefully monitored for safety and efficacy by the National Institute of Health (NIH) and the FDA.

EVIDENCE FROM PREVIOUS RESEARCH

Peer-reviewed and published data from four different animal species, eight different TBI injury models, and at least twelve different established laboratories have reported that hyperbaric oxygen treatment (HBOT) had an effect both on proximal outcome measures of efficacy such as ICP, cellular apoptosis, mitochondrial function and neurologic recovery in acute TBI in pre-clinical models.¹⁻¹³

These findings have been replicated in two human observational studies^{14,15} and 6 early phase II human studies of severe TBI.¹⁶⁻²² In a study that examined the effect of HBO on clinical outcome, PI Gaylan Rockswold et al randomized 168 TBI subjects with a GCS of 3 to 8 to HBO2 versus standard of care. They found that within this cohort, mortality in the HBOT group was 17%, whereas mortality in the control group was 32% (a 47% reduction in mortality). This treatment effect was more pronounced in subjects with a GCS of 4 to 6 (n=80). Among these subjects, mortality in the HBOT group was 17%, whereas mortality in the control group was 42% (a 60% reduction in mortality).

This FDA Phase 2 HOBIT trial seeks to replicate these findings, both for improvement patient outcomes and to determine the optimal treatment parameters of hyperbaric oxygen that are likely to result in the best improved neurologic outcome ~~in~~ for a subsequent phase 3 trial.

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